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Cardiovascular and Renal Outcomes in an Excellent Chronic Kidney Disease Clinic Compared with an Outpatient Clinic in a Primary Care Setting: A Retrospective Cohort Study

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Keywords

 $\label{eq:chronic kidney disease} Chronic kidney disease \cdot Multidisciplinary care \cdot \\ Multifactorial intervention$

Abstract

Background: Chronic kidney disease (CKD) is associated with increased cardiovascular morbidity and mortality. In standard care, the physician attempts to control all known risk factors, but treatment goals are achieved with difficulty. Assistance by a multidisciplinary care team may improve outcomes. Objective: To compare the cardiovascular and renal endpoints between patients with CKD receiving care from excellent CKD and outpatient clinics. Methods: A retrospective cohort study was conducted in a primary care setting in Thailand. Patients with CKD stages 3 and 4 in excellent CKD (n = 96) and outpatient clinics (n = 192) were matched in a 1:2 ratio with the propensity score. We collected data from electronic medical records concerning the incidences of primary composite outcomes including rapid renal progression, end-stage renal disease, myocardial infarction, congestive heart failure, stroke, and mortality. Multidisciplinary team care in the excellent CKD clinic consisted of physician, nurse, pharmacist, dietitian, physical therapist, and applied Thai traditional physician. The outpatient clinic consisted of physician care only. **Results:** Subjects' mean age

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E-Mail karger@karger.com www.karger.com/kdd was 64.54 ± 10.96 years, and 52.1% were female. During an average 49.63 ± 8.36 months of follow-up, 74 events occurred including 35 (47.30%) patients who experienced renal events, 29 (39.19%) who experienced cardiovascular events, and 10 (13.51%) who experienced loss of life. The Kaplan-Meier curve indicated a higher percentage of subjects without primary composite outcomes in the excellent CKD clinic than those in the outpatient clinic (66.85%; 95% Cl 0.48–0.80 vs. 44.71%; 95% Cl 0.29–0.60; *p* = 0.005). From multivariate analysis, the excellent CKD clinic group had a 64% lower risk for primary composite outcomes compared with those in the outpatient clinic (adjusted HR 0.36; 95% CI 0.18–0.74; p = 0.005). **Conclusion:** A multidisciplinary care system can reduce composition outcomes including cardiovascular and renal outcomes for the growing CKD population. The optimal outcomes arise from the medical personnel's teamwork, not from one physician alone.

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Introduction

Chronic kidney disease (CKD) has a high global prevalence creating high economic costs to health systems including in Thailand [1, 2]. Continuous worsening of kidney function in CKD is associated with increased risks of

Noppawit Aiumtrakul, MD 315, Department of Military and Community Medicine Phramongkutklao College of Medicine Bangkok 10400 (Thailand) E-Mail tan.niie@me.com cardiovascular morbidity and mortality [3]. CKD can progress to end-stage renal disease (ESRD), requiring renal replacement therapy [4]. In Thailand, the prevalence of renal replacement therapy has been rising rapidly from 30 per million population in 1997 to 1,200 per million population in 2014. To stem the rapidly increasing prevalence of type 2 diabetes, obesity, and hypertension that may predispose the development of CKD, preventive strategies constitute weight loss interventions, effective therapies for hypertension and diabetes by diet and lifestyle changes, pharmacological therapy, or surgical interventions and cost-effective measures [5].

It has been suggested that therapeutic interventions at the initial stage of disease would be one method to reduce the risk of ESRD and cardiovascular complications in CKD [6]. However, growing evidence indicates that primary care physicians show significant variation in their ability to recognize CKD stages regarding the unawareness in using the glomerular filtration rate (GFR) estimating equation [7] and suboptimal management of CKD that might be developed. Late nephrology referral has been associated with increased mortality and morbidity, and early referral of patients with CKD to knowledgeable nephrologists was associated with improved pre-dialysis care and reduced hospitalization and mortality [8,9]. Difficulties in providing clinical care for patients with CKD causes required interventions involving a multidisciplinary care team.

Apart from standard treatment according to CKD clinical practice guidelines, we have focused on patient's knowledge and awareness, lifestyle modification, medical treatment, physical training program, acupuncture, and substitution of nonsteroidal anti-inflammatory drugs (NSAIDs) for pain control. Thus, early recognition and using an intensive multifactorial approach in primary care settings are important and beneficial [10, 11]. We, therefore, aimed to compare the treatment effectiveness for patients with CKD between multidisciplinary care in an excellent CKD clinic and usual care in an outpatient clinic of a primary care hospital in Thailand.

Materials and Methods

Subjects

This research comprised a 4-year retrospective cohort study conducted in a primary care hospital in Thailand. Recruitment began in January 2013 and continued until the end of January 2017 (Fig. 1). The study protocol was approved by the Institutional Review Board of the Royal Thai Army Medical Department's committee on human research.

Electronic medical records of patients with CKD aged more than 18 years with estimated GFR (eGFR) <60 mL/min/1.73 m² in the excellent CKD and outpatient clinics in a primary care setting were reviewed. Exclusion criteria were as follows: having hospitalization, malignancy, acquired immunodeficiency disorder, pregnancy, acute kidney injury, and ESRD within 3 months at the time of recruitment. The subjects in the excellent CKD clinic were matched one to two with subjects in the outpatient clinic, on the basis of their propensity score including age, sex, systolic blood pressure (BP), diastolic BP, and eGFR. Finally, 288 subjects (96 subjects in the excellent CKD clinic and 192 subjects in the outpatient clinic) were included in our study. To study the effect of treatment on CKD, between patients who were treated in the CKD clinic and in the standard outpatient department were referred to the Effectiveness of Integrated Care on Delaying Progression of stage 3-4 Chronic Kidney Disease in Rural Communities of Thailand (ESCORT study) [12]. The sample size needed 433 patients in the CKD clinic and 255 patients in the standard outpatient clinic.

Outpatient Clinic

Outpatient clinic group treatment consisted of care under a general practitioner alone. Subjects in this group were managed according to the general practitioner's knowledge based on Thai CKD clinical practice guidelines. The average follow-up time in this group was every 3 months.

Excellent CKD Clinic

The excellent CKD clinic multidisciplinary team consisted of a general practitioner, nurse practitioner, dietitian, physical therapist, psychologist, pharmacist, medical technologist, and applied Thai traditional physician. Subjects in this group were followed up monthly. Apart from standard management following Thai CKD clinical practice guidelines, clinical care in the excellent CKD clinic focused on patient's knowledge and awareness, lifestyle modification, medical management, physical training program, and substitution of NSAIDs by applied Thai traditional medicine for pain control, including traditional Thai massage with a bag of heated Thai medical herbs and acupuncture.

Lifestyle modification included diet counseling, exercise for weight reduction, and smoking cessation. For long-term compliance, financial counseling was introduced to the patients with CKD and their family members by the nurse practitioner, especially for subjects who had financial problems. In case of poor compliance, the excellent CKD clinic team would offer support by direct call for follow-up or home visit. Moreover, an eGFR online reporting system included a pop-up notification on the prescription page to optimize medical care. After the clinical care session, the multidisciplinary team always met to discuss any severe cases for individualized management or a plan to refer to a specialist.

Data Collection

The data was obtained by reviewing electronic medical records from the hospital database. At baseline, information on age, sex, body mass index (BMI), BP, underlying disease including type 2 diabetes, hypertension, and dyslipidemia, laboratory data including eGFR, serum creatinine, blood urea nitrogen (BUN), hemoglobin, hemoglobin A1c, and urine dipstick for microalbuminuria, and all medications including antihypertensive agents, lipid lowering agents, antiplatelet agents, and antihyperglycemic agents were recorded. Only medications which were prescribed over 6 months



Fig. 1. Enrollment flowchart. Primary composite outcome included the incidences of myocardial infarction, congestive heart failure, stroke, end-stage renal disease (ESRD), rapid renal progression, and all-cause mortality. AKI, acute kidney injury; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HT, hypertension; T2DM, type 2 diabetes mellitus.

during the recruitment period were defined at baseline. eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

Primary and Secondary Outcomes

Primary composite outcomes of the study included rapid renal progression, ESRD, coronary heart disease, congestive heart failure, any type of cerebrovascular disease, and all-cause mortality. Rapid renal progression was defined as a decline in eGFR over 25% from baseline annually or over 5 mL/min/1.73 m² annually among those without ESRD [13]. ESRD was defined as eGFR lower than 15 mL/min/1.73 m² or initiation of renal replacement therapy. International Classification of Diseases 10 (ICD-10) codes were identified in the hospital database to collect the outcome including coronary heart disease (either non-ST, ST elevation myocardial infarction, or unstable angina), congestive heart failure, and any type of cerebrovascular disease (transient ischemic attack, ischemic stroke, hemorrhagic stroke, and intracerebral hemorrhage). For secondary outcome, clinical and laboratory data were collected at the end of the study including frequency of hospitalization, changes in eGFR and serum creatinine, and changes in albuminuria.

Statistical Analyses

The continuous data were reported as means and standard deviation and categorical data were reported as number with percentage (%). The differences in continuous and categorical variables between the two groups were tested by Student's t test (or Mann-Whitney U test) and the χ^2 test (or Fisher's exact test), respectively. The Kaplan-Meier model and log-rank statistics were used to analyze primary composite outcome (rapid renal progression, ESRD, coronary heart disease, congestive heart failure, any type of cerebrovascular disease, and all-cause mortality). A multivariate analysis of multifactorial intervention on primary composite outcomes was calculated with the hazard ratio (HR) with 95% confidence intervals (CI), involving survival time to the first event in any individual subject. Cox regression model was performed to predict primary composite outcome and dropout after adjusting for sex, age, renal function, BP, hemoglobin A1c, BMI, use of ACEIs or ARBs, and comorbid diseases. All p values were twosided, and a *p* value < 0.05 was set to indicate statistical significance. All analyses were performed using SPSS 22.0 (SPSS, Chicago, IL, USA).

Variables	Outpatient clinic $(n = 192)$	Excellent CKD clinic $(n = 96)$	<i>p</i> value	
Age, years	64.54±11.48	64.54±9.9	1.000	
Female	104 (54.2)	46 (47.9)	0.317	
BMI	25.84±4.87	25.03±4.46	0.215	
Systolic BP, mm Hg	136.84±18.19	137.83±17.85	0.685	
Diastolic BP, mm Hg	78.09±12.94	75.55±10.93	0.127	
Hypertension	134 (69.8)	67 (69.8)	1.000	
Dyslipidemia	103 (53.6)	56 (58.3)	0.451	
Type 2 diabetes	82 (42.7)	45 (46.9)	0.502	
Hemoglobin A1c, %	7.8 ± 1.96	7.78±1.78	0.935	
Hemoglobin, g/dL	11.39 ± 2.23	11.32±1.96	0.801	
Mean eGFR, mL/min/1.73 m^2	39.88±12.06	39.16±12.55	0.639	
CKD stage 3	152 (79.2)	63 (65.6)	0.123	
CKD stage 4	40 (20.8)	26 (27.1)	0.123	
Serum creatinine, mg/dL	1.69±0.56	1.72 ± 0.44	0.637	
BUN, mg/dL	21.74±13.58	23.64±11.16	0.253	
Medications				
ACEI or ARBs	57 (29.7)	37 (38.5)	0.131	
Statin	92 (47.9)	55 (57.3)	0.134	
Aspirin	116 (60.4)	51 (53.1)	0.237	
Beta-blocker	51 (26.6)	28 (29.2)	0.641	
Calcium channel blocker	75 (39.1)	47 (49)	0.109	
Metformin	38 (19.8)	12 (12.5)	0.124	
Sulfonylurea	28 (14.6)	7 (7.3)	0.074	
Follow-up time, years	4.09±0.66	4.22±0.76	0.141	
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Table 1. Baseline characteristics with propensity matched between outpatient clinic and excellent CKD clinic groups

Data presented as mean \pm SD and *n* (%). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BUN, blood urea nitrogen; BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; CKD stage 3, eGFR between 30 and 59 mL/min/1.73 m²; CKD stage 4, eGFR between 15 and 29 mL/min/1.73 m².

Results

In total, 288 subjects (96 subjects in the excellent CKD clinic group and 192 subjects in the outpatient clinic group) with a mean age of 64.54 ± 10.96 years were included. Mean follow-up time was 49.63 ± 8.36 months for the entire cohort. The excellent CKD clinic and the outpatient clinic groups had similar characteristics at base-line regarding age, sex, BMI, eGFR, systolic BP, diastolic BP, hemoglobin A1c, hemoglobin, and the percentage of underlying diseases such as hypertension, type 2 diabetes, and dyslipidemia (Table 1).

Changes in Renal Function and Metabolic Parameters between Groups

Table 2 shows the changes in eGFR and laboratory results between the two groups. Compared with the outpatient clinic group, the excellent CKD clinic group had a lower annual decline in eGFR (-0.06 [-2.89, 2.77] vs. 8.17 [5.7, 10.65] mL/min/1.73 m²/year, p < 0.001) with a mean difference of -8.24 (-12.25, -4.22) and a lower percentage of decline in GFR (0.42% [-1.6, 2.44] vs. 4.76% [2.89, 6.62] per year, p = 0.005) with a mean difference of -4.34 (-7.32, -1.35). Moreover, the excellent CKD clinic group had a significantly lower rate of reducing BMI (-0.26 [-0.68, 0.15] vs. -0.97 [-1.45, -0.49] per year, p = 0.037) with a mean difference of about 0.71 (0.04, 1.37). There were no significant differences in the changes in serum creatinine, BUN, BP, hemoglobin A1c, and hemoglobin between the two groups.

Clinical Outcomes between Groups

A total of 16 (16.5%) subjects in the excellent CKD clinic group and 58 (19.9%) subjects in the outpatient clinic group had an event of primary composite outcome including rapid renal progression, ESRD, coronary heart

	Outpatient clinic $(n = 291)$	Excellent CKD clinic ($n = 96$)	Mean differences	<i>p</i> value
Mean changes of laboratory results				
Decline in eGFR, mL/min/1.73 m ²	8.17 (5.70, 10.65)	-0.06 (-2.89, 2.77)	-8.24 (-12.25, -4.22)	< 0.001
% decline in eGFR per year	4.76 (2.89, 6.62)	0.42 (-1.6, 2.44)	-4.34 (-7.32, -1.35)	0.005
Serum creatinine, mg/dL	0.32 (0.03, 0.61)	0.17 (-0.03, 0.38)	-0.14 (-0.58, 0.29)	0.512
BUN, mg/dL	5.79 (2.68, 8.9)	4.94 (0.29, 9.59)	-0.85 (-6.2, 4.5)	0.753
Systolic BP, mm Hg	-1.42 (-5.59, 2.76)	-5.14 (-9.43, -0.85)	-3.72 (-10.28, 2.84)	0.265
Diastolic BP, mm Hg	-3.75 (-6.53, -0.98)	-3.97 (-6.94, -1.00)	-0.22 (-4.62, 4.18)	0.922
Hemoglobin A1c, %	0.89 (0.41, 1.37)	0.32 (-0.09, 0.73)	-0.57 (-1.26, 0.12)	0.106
Hemoglobin, g/dL	-0.95 (-1.37, -0.54)	-0.38 (-0.95, 0.19)	0.57 (-0.17, 1.31)	0.127
BMI	-0.97 (-1.45, -0.49)	-0.26 (-0.68, 0.15)	0.71 (0.04, 1.37)	0.037
Clinical outcomes				
Primary composite outcome	58 (19.9)	16 (16.7)	-	0.013
Mortality rate	17 (5.84)	2 (2.1)	-	0.029
End-stage renal disease	25 (8.59)	8 (8.3)	-	0.239
50% decline in eGFR	21 (7.22)	8 (8.3)	-	0.489
Rapid renal progression	23 (7.90)	10 (10.4)	-	0.013
Coronary heart disease	3 (0.01)	0 (0)	-	0.218
Congestive heart failure	8 (2.74)	1(1)	-	0.151
Cerebrovascular disease	18 (6.18)	5 (5.2)	-	0.219
Hospitalizations per year	1 (0, 2.5)	1 (0, 2)	-	0.299

Table 2. Mean changes per year in laboratory measurements and clinical outcomes between outpatient clinic and excellent CKD clinic groups

Data presented as mean change (95% CI) and n (%). BUN, blood urea nitrogen; BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate.



Fig. 2. Kaplan-Meier curve of patient outcomes between outpatient and excellent CKD clinic. **a** Kaplan-Meier curve of primary composite outcomes between outpatient and excellent CKD clinics (log-rank test <0.005). Primary composite outcomes include rapid renal progression, end-stage renal disease, coronary heart

disease, congestive heart failure, any type of cerebrovascular disease, and all-cause mortality. **b** Kaplan-Meier curve of patient survival (all-cause mortality) between outpatient and excellent CKD clinics (log-rank test = 0.019).

Variables	Univariate		Multivariate	
	crude HR (95% CI)	<i>p</i> value	adjusted HR [#] (95% CI)	<i>p</i> value
Age (years)	1.02 (1.00, 1.04)	0.071		
eGFR (mL/min/1.73 m ²)	0.98 (0.96, 0.99)	0.049	1.00 (0.97, 1.04)	0.912
Serum creatinine (mg/dL)	1.72 (1.20, 2.48)	0.003		
Female	1.51 (0.93, 2.44)	0.096		
Type 2 diabetes	1.15 (0.73, 1.82)	0.548		
Hypertension	0.64 (0.39, 1.03)	0.065		
Dyslipidemia	0.93 (0.59, 1.47)	0.751		
BMI	0.98 (0.93, 1.03)	0.447		
Systolic BP (mm Hg)	1.02 (1.00, 1.03)	0.015	1.01 (1.00, 1.03)	0.133
Diastolic BP (mm Hg)	1.01 (0.99, 1.03)	0.232		
Hemoglobin (g/dL)	1.07 (0.95, 1.21)	0.277		
Hemoglobin A1c (%)	1.24 (1.10, 1.40)	0.001	1.35 (1.13, 1.60)	0.001
BUN (mg/dL)	1.02 (1.01, 1.04)	0.001	1.02 (1.00, 1.04)	0.102
ACEI or ARBs	0.43 (0.24, 0.78)	0.005	0.41 (0.19, 0.89)	0.025
Statin	0.86 (0.55, 1.36)	0.519		
Aspirin	1.16 (0.73, 1.87)	0.531		
Beta-blockers	1.07 (0.66, 1.74)	0.788		
Calcium channel blockers	0.76 (0.48, 1.22)	0.263		
Metformin	0.61 (0.31, 1.19)	0.146		
Sulfonylurea	1.02 (0.51, 2.06)	0.949		
Excellent CKD clinic	0.46 (0.26, 0.80)	0.006	0.36 (0.18, 0.74)	0.005

Table 3. Cox regression model of excellent CKD clinic versus outpatient clinic groups for primary compositeoutcomes

All variables are at baseline level. Primary composite outcomes include rapid renal progression, ESRD, coronary heart disease, congestive heart failure, any type of cerebrovascular disease, and all-cause mortality. [#] Adjusting for baseline eGFR, systolic BP, hemoglobin A1c, BUN, and use of ACEIs or ARBs. ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BUN, blood urea nitrogen; BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

disease, congestive heart failure, any type of cerebrovascular disease, and all-cause mortality (p = 0.013). Kaplan-Meier analysis illustrated a lower primary composite outcome in the excellent CKD clinic group than the outpatient clinic group (log-rank test, p = 0.005) (Fig. 2a). Cox regression analysis revealed that the risk of primary composite outcome in the excellent CKD clinic group was reduced to 61% compared with the outpatient clinic group (HR 0.46; 95% CI 0.26–0.8; p = 0.006). After adjusting for eGFR, systolic BP, hemoglobin A1c, BUN, and use of ACEIs or ARBs, the HR persisted significantly at HR 0.39 (95% CI 0.19–0.80; p = 0.010) (Table 3).

As for all-cause mortality, a total of 2 (2.10%) subjects in the excellent CKD clinic group and 17 (5.84%) subjects in the outpatient clinic group died (p = 0.029). Kaplan-Meier analysis illustrates a higher survival rate in the excellent CKD clinic group than the outpatient clinic group (log-rank test, p = 0.019) (Fig. 2b). Cox regression analysis revealed that the risk of death in the

excellent CKD clinic group was significantly reduced compared with the outpatient clinic group (HR 0.21; 95% CI 0.05–0.89; p = 0.035). After adjusting for age and mean eGFR, the HR persisted significantly at HR 0.22 (95% CI 0.05–0.95; p = 0.043) (Table 4). However, the significant outcomes were not found in the incidence of 50% decline in eGFR, ESRD, coronary heart disease, congestive heart failure, any type of cerebrovascular disease, and hospitalization.

Discussion

The 4-year retrospective cohort study showed that the multidisciplinary care team in the excellent CKD clinic of primary care setting improved patient outcomes among patients with CKD including composite outcome, all-cause mortality, and hospitalization rate. The better survival outcomes and hospitalization rate in the

Variables	Univariate		Multivariate	
	crude HR (95% CI)	<i>p</i> value	adjusted HR [#] (95% CI)	<i>p</i> value
Age (years)	1.05 (1.00, 1.09)	0.040	1.05 (1.01, 1.09)	0.025
eGFR (mL/min/1.73 m ²)	1.01 (0.97, 1.05)	0.532	1.02 (0.98, 1.06)	0.327
Serum creatinine (mg/dL)	0.38 (0.11, 1.31)	0.125		
Female	1.68 (0.64, 4.43)	0.292		
Type 2 diabetes	1.19 (0.48, 2.93)	0.712		
Hypertension	0.64 (0.25, 1.63)	0.348		
Dyslipidemia	1.34 (0.53, 3.41)	0.535		
BMI	0.98 (0.87, 1.09)	0.69		
Systolic BP (mm Hg)	1.01 (0.99, 1.04)	0.258		
Diastolic BP (mm Hg)	1.00 (0.96, 1.04)	0.955		
Hemoglobin (g/dL)	0.90 (0.72, 1.13)	0.37		
Hemoglobin A1c (%)	1.25 (1.00, 1.57)	0.051		
BUN (mg/dL)	1.01 (0.98, 1.04)	0.58		
ACEI or ARBs	0.52 (0.17, 1.56)	0.243		
Statin	1.07 (0.43, 2.62)	0.89		
Aspirin	1.47 (0.56, 3.86)	0.438		
Beta-blockers	0.45 (0.13, 1.54)	0.204		
Calcium channel blockers	1.37 (0.56, 3.37)	0.494		
Metformin	0.77 (0.22, 2.64)	0.677		
Sulfonylurea	0.79 (0.18, 3.43)	0.752		
Excellent CKD clinic	0.21 (0.05, 0.89)	0.035	0.22 (0.05, 0.95)	0.043

Table 4. Cox regression model of excellent CKD clinic versus outpatient clinic groups for all-cause mortality

All variables are at baseline level. [#] Adjusting for baseline age and eGFR. ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BUN, blood urea nitrogen; BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

present study were similar to related studies [11, 14]. Many explanations could explain the improvement in these outcomes. The present study supported the hypothesis that a multifactorial intervention directed at multiple treatment targets is effective even when achieving only modest improvements. Our excellent CKD clinic facilitated a holistic approach among patients with CKD improving patients' attitudes and knowledge levels regarding CKD. A study by Wu et al. [10] revealed that a reduced mortality rate was associated with education programs in pre-dialysis patients with CKD. Physical training programs also played a crucial role in survival outcome. One related study showed a significant relationship between physical inactivity and increase in mortality rate [15]. Smoking cessation [16] and effective medical prescription, especially statin [17] and RAAS blockers [18], were significantly associated with cardiovascular and survival benefit among patients with CKD as well. Better cooperation was noted in diet modification, medical compliance, avoidance of nephrotoxic drugs including NSAIDs and herbal medications, substitution of NSAIDs by applied Thai traditional medicine for pain control, increased follow-up frequency, financial counseling for long-term treatment plans, and direct personal calling for poor compliance patients. Although these parameters were not measured directly, it might have an effect on the outcomes.

The excellent CKD clinic might also prevent a decline in eGFR, and this result was correlated to related studies [19, 20]. However, renal events including 50% decline in eGFR and ESRD did not significantly differ between the two groups. Moreover, this study also revealed nonsignificant differences between the two patient groups regarding cardiovascular events, for which the results were the same as in related studies [14, 21].

The present study did not exhibit differences in changes in serum creatinine, BUN, systolic and diastolic BP, hemoglobin A1c, hemoglobin, and standard medications including ACEI/ARB and statins. RAAS blockers have been prescribed as first-line antihypertensive medication among patients with CKD to reduce albuminuria and improve renal and cardiovascular events [22]. Consequences of combining lifestyle modifications and more effective medication prescriptions by the multidisciplinary care team may have contributed to reducing allcauses mortality and composite outcome in the present study.

Several limitations were noted in the present study. First, the relatively small sample size of our cohort study is the main limitation of the study. Second, patient compliance and adherence to disease education intervention could not be evaluated completely in our retrospective study. Laboratory data were not collected and measured at all time points of follow-up. A systemic bias in laboratory measures possibly existed. We could not exclude that other unmeasured factors contributed to the efficacy of the multidisciplinary care team in the excellent CKD clinic group. Finally, the generalizability of our findings might be limited by the selection of relatively older patients with CKD and subjects living in urban areas of Thailand.

Conclusion

The multidisciplinary care team in the excellent CKD clinic in a primary care setting improved outcomes among patients with CKD including primary composite outcome and all-cause mortality. The excellent CKD clinic might also have prevented a decline in eGFR in the CKD population.

References

- 1 Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, et al. Global Prevalence of Chronic Kidney Disease - A Systematic Review and Meta-Analysis. PLoS One. 2016 Jul;11(7):e0158765.
- 2 Satirapoj B, Supasyndh O, Mayteedol N, Punpanich D, Chaiprasert A, Nata N, et al. Obesity and its relation to chronic kidney disease: a population-based, cross-sectional study of a Thai army population and relatives. Nephrology (Carlton). 2013 Mar;18(3): 229–34.
- 3 Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004 Sep;351(13): 1296–305.
- 4 Matsushita K, van der Velde M, Astor BC, Woodward M, Levey AS, de Jong PE, et al.; Chronic Kidney Disease Prognosis Consortium. Association of estimated glomerular filtration rate and albuminuria with all-cause

and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Lancet. 2010 Jun;375(9731):2073–81.

- 5 Hall ME, do Carmo JM, da Silva AA, Juncos LA, Wang Z, Hall JE. Obesity, hypertension, and chronic kidney disease. Int J Nephrol Renovasc Dis. 2014 Feb;7:75–88.
- 6 James MT, Hemmelgarn BR, Tonelli M. Early recognition and prevention of chronic kidney disease. Lancet. 2010 Apr;375(9722):1296– 309.
- 7 Israni RK, Shea JA, Joffe MM, Feldman HI. Physician characteristics and knowledge of CKD management. Am J Kidney Dis. 2009 Aug;54(2):238–47.
- 8 Stack AG. Impact of timing of nephrology referral and pre-ESRD care on mortality risk among new ESRD patients in the United States. Am J Kidney Dis. 2003 Feb;41(2):310– 8.
- 9 Smart NA, Titus TT: Outcomes of early versus late nephrology referral in chronic kidney

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Statement of Ethics

The study protocol has been approved by the Institutional Review Board of Royal Thai Army Medical Department's committee on human research.

Disclosure Statement

The authors declare that no potential conflict of interest exists.

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Author Contributions

N.A., K.E., and K.P. collected the data and reviewed the literature. N.A. and B.S. provided valuable input in study design and data collection and drafted the article and revised it critically. R.R. and W.K. provided literature review. All authors read and approved the manuscript and met the criteria for authorship.

> disease: a systematic review. Am J Med. 2011 Nov;124(11):1073-80.e2.

- 10 Wu IW, Wang SY, Hsu KH, Lee CC, Sun CY, Tsai CJ, et al. Multidisciplinary predialysis education decreases the incidence of dialysis and reduces mortality—a controlled cohort study based on the NKF/DOQI guidelines. Nephrol Dial Transplant. 2009 Nov;24(11): 3426–33.
- 11 Chen YR, Yang Y, Wang SC, Chiu PF, Chou WY, Lin CY, et al. Effectiveness of multidisciplinary care for chronic kidney disease in Taiwan: a 3-year prospective cohort study. Nephrol Dial Transplant. 2013 Mar;28(3): 671–82.
- 12 Jiamjariyapon T, Ingsathit A, Pongpirul K, Vipattawat K, Kanchanakorn S, Saetie A, et al. Effectiveness of Integrated Care on Delaying Progression of stage 3-4 Chronic Kidney Disease in Rural Communities of Thailand (ES-CORT study): a cluster randomized controlled trial. BMC Nephrol. 2017 Mar;18(1):83.

- 13 Beck L, Bomback AS, Choi MJ, Holzman LB, Langford C, Mariani LH, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for glomerulonephritis. Am J Kidney Dis. 2013 Sep;62(3):403–41.
- 14 Hemmelgarn BR, Manns BJ, Zhang J, Tonelli M, Klarenbach S, Walsh M, et al. Association between multidisciplinary care and survival for elderly patients with chronic kidney disease. J Am Soc Nephrol. 2007 Mar;18(3):993–9.
- 15 Beddhu S, Baird BC, Zitterkoph J, Neilson J, Greene T. Physical activity and mortality in chronic kidney disease (NHANES III). Clin J Am Soc Nephrol. 2009 Dec;4(12):1901–6.
- 16 Samet JM. The 1990 Report of the Surgeon General: The Health Benefits of Smoking Cessation. Am Rev Respir Dis. 1990 Nov;142(5): 993–4.
- 17 Shepherd J, Cobbe SM, Ford I, Isles CG, Lorimer AR, MacFarlane PW, et al.; West of Scotland Coronary Prevention Study Group. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. N Engl J Med. 1995 Nov;333(20):1301– 7.
- 18 Balamuthusamy S, Srinivasan L, Verma M, Adigopula S, Jalandhara N, Hathiwala S, et al. Renin angiotensin system blockade and cardiovascular outcomes in patients with chronic kidney disease and proteinuria: a metaanalysis. Am Heart J. 2008 May;155(5):791– 805.
- 19 Bayliss EA, Bhardwaja B, Ross C, Beck A, Lanese DM. Multidisciplinary team care may slow the rate of decline in renal function. Clin J Am Soc Nephrol. 2011 Apr;6(4):704–10.
- 20 Luciano EP, Luconi PS, Sesso RC, Melaragno CS, Abreu PF, Reis SF, et al. Prospective study of 2151 patients with chronic kidney disease under conservative treatment with multidisciplinary care in the Vale do Paraíba, SP. J Bras Nefrol. 2012 Jul-Sep;34(3):226–34.
- 21 van Zuilen AD, Bots ML, Dulger A, van der Tweel I, van Buren M, Ten Dam MA, et al. Multifactorial intervention with nurse practitioners does not change cardiovascular outcomes in patients with chronic kidney disease. Kidney Int. 2012 Sep;82(6):710–7.
- 22 Satirapoj B, Adler SG. Prevalence and Management of Diabetic Nephropathy in Western Countries. Kidney Dis (Basel). 2015 May; 1(1):61–70.